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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,312	04/13/2001	Lisbeth Illum	8567-603US (WESR/P21598US	2569

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/834,312	ILLUM ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7, 20, 21 and 28-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,20,21,28-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of amendment and remarks filed 04/05/04. Claims 7, 20, 21, 28-58 are pending and of these claims 40-58 are new.

Other Matters:

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 7, 20, 21, 28, 29, 34, 38, 39, 44, 45, 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 34 is consisting essentially of fexofenadine and cyclodextrin or glycofurol as recited in currently amended claim 34. However, depended claim 28 further comprises a gelling agent or a bioadhesive material that may affect the novel characteristic of the composition of claim 34. Correction is requested. It is suggested that claim 34 recite --- and optional gelling agent or bioadhesive---. Claim 28 may be cancelled or may recite the gelling agents and bioadhesive, with removal or deletion of the "further." Correction is respectfully requested.

Claim Rejections - 35 USC § 102

3. The rejection of claims 34 and 20 under 35 U.S.C. 102(b) as being anticipated by Carr et al. (US 4,254,129) is withdrawn because the fexofenadine composition of Carr does not contain cyclodextrin or glycofurol.

4. However, new claims 40 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Carr et al. (US 4,254,129).

Applicants' argument advanced for Carr states that Carr does not disclose aqueous vehicle such as water and propylene glycol; and that there is no disclosure in Carr that specifies the use of a pharmaceutical excipient that increases the solubility of fexofenadine or its salt.

5. Applicants' arguments filed 04/05/04 have been fully considered but they are not persuasive.

Carr discloses that fexofenadine, which is one of the compounds that satisfies the compounds of Carr can be "administered in injectable dosages by solution or suspension of the compound in a physiologically acceptable diluent with a pharmaceutically acceptable carrier" that "can be a sterile liquid such as water and oils, with or without the addition of surfactant and other pharmaceutically acceptable adjuvants;" and that water, saline, "aqueous dextrose and related sugar solution and glycols such as propylene glycol or polyethylene glycol are preferred liquid carriers for injectable solutions," (column 5, lines 46-52 and 55-59). This section of Carr goes to show that Carr discloses aqueous compositions where the aqueous vehicle is water, propylene glycol or polyethylene glycol. The composition of Carr can be administered to the nose, throat and bronchial tubes (column 5, lines 10-16). Increasing the solubility of the fexofenadine would be and is a function of the carrier or excipient and there is no distinction as to why the excipients or carriers of Carr, which are the one claimed, would not be effective in increasing the solubility of fexofenadine.

Claim Rejections - 35 USC § 103

6. The rejection of claims 30-33, 35 and 37 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Aslanian et al. (US 6,103,735) is

withdrawn because Aslanian does not disclose a composition that contains glycofurol or cyclodextrin.

7. However, new claims 40, 41, 49 and 50-57 remain rejected under 35 U.S.C. 102(e) as anticipated by Aslanian et al. (US 6,103,735).

Applicants argue that

a) Aslanian discloses liquid preparations that may contain propylene glycol and that Aslanian does not disclose other components for use in aqueous solutions or liquid formulations of the Aslanian compositions.

b) The claimed composition consists essentially of fexofenadine and a pharmaceutical excipient that increases the solubility of the fexofenadine and that Aslanian does not disclose glycofurol or cyclodextrin.

c) Aslanian does not teach the significance of increasing the solubility of fexofenadine in an aqueous solution that would have cause a person of ordinary skill to substitute the polyethylene glycol for other pharmaceutical excipients that increase the solubility of fexofenadine.

d) A teaching in Aslanian of 1-200 mg of H_1 antagonist does not suggest a concentration of 100 μm/ml to 100 mg/ml to be suitable concentration of fexofenadine for use in the eye or nose, and that water-propylene glycol solutions are disclosed as suitable for solutions for use in potential injections and oral solutions; that a person of ordinary skill in the art would come away from Aslanian that fexofenadine has a low solubility in water and there is nothing in Aslanian that points to a combination of water and propylene glycol to provide a solution that

would have sufficient amount of solubilized fexofenadine suitable for delivery to the eye and nose.

Thus, conclude applicants, Aslanian neither anticipates or renders obvious the claimed invention.

8. Applicants' arguments filed 04/05/04 have been fully considered but they are not persuasive.

On point a) examiner agrees with applicants that Aslanian discloses liquid preparations that may contain or contain propylene glycol and it is unclear what applicants mean by "does not disclose other component for use in aqueous or liquid formulations." What other components are applicants referring to? It is clear that Aslanian discloses fexofenadine in liquid preparations including solutions, suspensions and emulsions in water or water-propylene glycol solutions for parenteral and intranasal administration (column 6, lines 56-60). On point b), it is noted that claim 34 which is a compositions that consists essentially of ... is not rejected over Aslanian, so also is claim 35 that no longer recite propylene glycol; the claimed composition of claims 40 and 41 however still comprises and continue to recite propylene glycol. On point c) Aslanian does not have to teach the significance of increasing the solubility of fexofenadine because the reason for making any water-insoluble or partially water-soluble drugs soluble or more soluble would be apparent to a person of skill or a person of ordinary skill in the art. Secondly, the carriers propylene glycol, glycofurol and cyclodextrin are said to increase the solubility of fexofenadine and thus those carriers would inherently increase the solubility of fexofenadine except applicants have a knowing that the propylene glycol of Aslanian would not increase the solubility of fexofenadine, and this would appear to be contrary to what applicants claim. On point d), μm in

100 μm/ml to 100 mg/ml may be a typographical error of ng/ml. However, Aslanian's disclosure that water-propylene glycol solutions are suitable for parenteral injections and oral solutions is a disclosure that water-propylene glycol solutions containing the drugs of interest such as fexofenadine are suitable and this disclosure would lead a person of skill or of ordinary skill in the art to use such a solution or suspension with the eye or nose since Aslanian discloses a method of using the composition to treat allergic rhinitis, asthma and related disorders. Therefore, the rejection is maintained over the new claims.

9. Claims 42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aslanian et al. (US 6,103,735). This new rejection is necessitated by the new claims from the amendment.

Aslanian discloses the composition and methods of the instant claims. Aslanian does not specifically disclose how much excipient is used, that is when the excipient is defined as propylene glycol. However, where the general conditions of a subject matter are taught or encompassed in the prior art, differences in amounts of excipients will not support the patentability of the subject matter over the prior art unless there is evidence indicating such amount is critical to the composition and it is not inventive to discover optimum workable amounts by routine experimentation. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare and use the formulation of Aslanian containing propylene glycol excipient. One having ordinary skill in the art would have been motivated to optimize the amount of propylene glycol excipient with the expectation of producing a composition that would be suitable for administration to the eye and nose.

10. The rejection of claims 30-33, 35 and 37 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hwang et al. (US 6,451,815) is withdrawn the claimed composition no longer contains propylene glycol in view of the current amendment.

11. However, claims 40, 41, 49-57 are rejected under 35 U.S.C. 102(e) as anticipated by Hwang et al. (US 6,451,815).

Applicants argue:

a) Hwang discloses composition that contains fexofenadine (when the R in the formula is hydrogen) and p-glycoprotein inhibitor in solution or suspension, and the solution or suspension of fexofenadine may further comprise propylene glycol; that no other pharmaceutical excipients that increase the solubility of fexofenadine in water are taught; there is no disclosure in Hwang where aqueous composition containing fexofenadine and propylene glycol are taught because the examples of fexofenadine and propylene glycol are formulated as solid tablet for oral administration.

b) Hwang does not render the claims obvious because one element of the instant claim is missing; no suggestion of the missing element is provided by Hwang; one of ordinary skill in the art would not have been motivated to modify the teachings of Hwang to arrive at the claimed invention; no suggestion by Hwang of the need or desire to increase the solubility of fexofenadine in water and the examples provided are all solid formulations; no motivation is provided by Hwang to seek to use cyclodextrin or glycofurol to increase the solubility of fexofenadine.

12. Applicants' arguments filed 04/05/04 have been fully considered but they are not persuasive.

On point a), no other excipient is necessary and propylene glycol is that claimed excipient in new claims 40 and 41. Examples are exemplification of specific disclosed embodiments and all the varied embodiments of the disclosed work need not be exemplified. Examples are what they are, examples and it is sufficient that the prior art disclose the subject matter of the claimed invention.

On point b), the new claims recite propylene glycol as one of the excipients equivalent to cyclodextrin and glycofurol and Hwang only has to disclose one of the three excipients recited in new claims 40 and 41. Also, the carriers propylene glycol, glycofurol and cyclodextrin are said to increase the solubility of fexofenadine and thus those carriers would inherently increase the solubility of fexofenadine except applicants have a knowing that the propylene glycol of Hwang would not increase the solubility of fexofenadine, and this would appear to be contrary to what applicants claim. Since Hwang discloses propylene glycol and the claims recite propylene glycol, there is no need for the person of ordinary skill in the art to want to substitute propylene glycol with glycofurol or cyclodextrin.

13. Claims 42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hwang et al. (US 6,451,815). This new rejection is necessitated by the new claims from the amendment.

Hwang discloses the composition and methods of the instant claims. Hwang does not specifically disclose how much excipient is used, that is when the excipient is defined as propylene glycol. However, where the general conditions of a subject matter are taught or

encompassed in the prior art, differences in amounts of excipients will not support the patentability of the subject matter over the prior art unless there is evidence indicating such amount is critical to the composition and it is not inventive to discover optimum workable amounts by routine experimentation. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare and use the formulation of Hwang containing propylene glycol excipient. One having ordinary skill in the art would have been motivated to optimize the amount of propylene glycol excipient with the expectation of producing a composition that would be suitable for administration to the eye and nose.

14. The rejection of claim 21 under 35 U.S.C. 103(a) as being unpatentable over Carr et al. (US 4,254,129) in view of Hwang et al. (US 6,451,815) is withdrawn because the generic claim 34 from which it depends does not recite propylene glycol in light of the amendment. Argument is thus moot.

15. The rejection of claims 28, 29, 38 and 39 rejected under 35 U.S.C. 103(a) as being unpatentable over Carr et al. (US 4,254,129) in view of Hwang et al. (6,451,815) is withdrawn because the generic claim 34 from which it depends does not recite propylene glycol in light of the amendment. Argument is thus moot.

16. The rejection of claims 35 and 36 under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 6,267,985) is withdrawn because applicants' argument is persuasive.

17. Claims 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carr et al. (US 4,254,129). This new rejection is necessitated by the new claims from the amendment.

Carr discloses the composition and methods of the instant claims. Carr does not specifically disclose how much excipient is used, that is when the excipient is defined as

propylene glycol. However, where the general conditions of a subject matter are taught or encompassed in the prior art, differences in amounts of excipients will not support the patentability of the subject matter over the prior art unless there is evidence indicating such amount is critical to the composition and it is not inventive to discover optimum workable amounts by routine experimentation. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare and use the formulation of Carr containing propylene glycol excipient. One having ordinary skill in the art would have been motivated to optimize the amount of propylene glycol excipient with the expectation of producing a composition that would be suitable for administration to the eye and nose.

18. Claims 35-37, 30-33, 41, 46, 52-54 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magee et al. (US 2002/0111495).

Magee discloses pharmaceutical composition that comprises phosphodiesterase inhibitor (abstract, paragraph [0668] and [0669] on page 9), therapeutic agent such as fexofenadine (paragraph [0218], [0625] and claim 22) and poloxamer, cyclodextrin and propylene glycol (paragraph [0688], [0691], [0693], [0694]). Water can also be a solvent or carrier in the composition (paragraph [0694], [0699], [0795] and [0710]). The composition can be administered topically to the skin or eye (paragraph [0703]) and the composition is a controlled release or sustained release composition (paragraph [0706]). The composition of Magee may also be "administered by nasal aerosol or inhalation through the use of nebulizer, a dry powder inhaler or a metered dose inhaler." Hydroxypropyl-β-cyclodextrin is a derivative of β-cyclodextrin and would be an obvious form of cyclodextrin for use.

Instant claim 35 is directed to a composition that comprises fexofenadine and pharmaceutical excipient that is selected from the group consisting of cyclodextrin and glycofurol. The comprising language of the claim allows for the presence of the phosphodiesterase inhibitor or does not exclude the presence of the phosphodiesterase inhibitor in the composition. Thus, Magee discloses the instant composition and administers the composition topically to the eye or skin. Magee does not disclose amounts of fexofenadine that can be present in the composition as recited in instant composition 35. However, where the general conditions of a subject matter are taught or encompassed in the prior art, differences in amounts of active agents will not support the patentability of the subject matter over the prior art unless there is evidence indicating such amount is critical to the composition and it is not inventive to discover optimum workable amounts by routine experimentation. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare and use the formulation of Magee containing cyclodextrin and propylene glycol and fexofenadine and phosphodiesterase inhibitor. One having ordinary skill in the art would have been motivated to optimize the amount of fexofenadine with the expectation of producing a composition that would be suitable for administration to the eye or nose.

19. Claims 34, 7, 20, 21, 28, 29, 38, 39, 40, 44, 45 and 47-51 rejected under 35 U.S.C. 103(a) as being unpatentable over Carr et al. (US 4,254,129) in combination with Magee et al. (US 2002/0111495).

The teachings of Carr are disclosed above. Hydroxypropyl-β-cyclodextrin is a derivative of β-cyclodextrin and would be an obvious form of cyclodextrin for use. Carr fails to disclose that the fexofenadine composition contains cyclodextrin. Magee is discussed above to

disclose pharmaceutical composition containing fexofenadine, cyclodextrin or propylene glycol or poloxamer. Thus Magee is relied on for a teaching that fexofenadine containing composition can be formulated with cyclodextrin and poloxamer and propylene glycol. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the fexofenadine composition of Carr in which fexofenadine is combined with propylene glycol and other excipients. One having ordinary skill in the art would have been motivated to prepare the fexofenadine composition where the excipient is cyclodextrin as disclosed by Magee with the expectation that the cyclodextrin would sequester the fexofenadine and where the fexofenadine would be available for sustained or controlled release and delivery.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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